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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/827,498 | 04/19/2004 | Liangjing Chen | 6560US | 3464 |

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| EXAMINER | |
|---|---|
| HUTSON, RICHARD G | |

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| 1652 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/827,498 | CHEN ET AL. | |
| | Examiner | Art Unit | |
| | Richard G. Hutson | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 9/26/2007.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1,5-9,11-28,84-98,102-112,115-125 and 127-129 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,5-9,11-28,84-98,102-112,115-125 and 127-129 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's cancellation of claims 2-4, 46-60, 113, 114, amendment of claims 1, 9, 11, 84-88, 97, 98, 102, 103, 115, 127 and the addition of new claim 129, in the paper filed on 9/26/2007, is acknowledged. Claims 1, 5-9, 11-28, 84-98, 102-112, 115-125 and 127-129 are still at issue and are present for examination.

Applicants' arguments filed on 9/26/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### *Claim Objections*

Claim1 is objected to because of the following informalities: Claim 1 recites "M-MLV". It is suggested that the first time M-MLV is used in the claims it be preceded by the abbreviated phrase written out in full.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-9, 11-28, 84-98, 102-112,115-125 and 127-129 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 5-9, 11-28, 84-98, 102-112,115-125 and 127-129 are indefinite in that it recites a hyperactive reverse transcriptase comprising or corresponding to H638 or F155, without an amino acid sequence for reference. As "H638" and "F155" are relative terms, their recitation in the claims is unclear and indefinite without the amino acid sequence to which they are relative.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-9, 11-28, 84-98, 102-112,115-125 and 127-129 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 1-9, 11-28, 46-60, 84-98, 102-125 and 125-128. In response to this rejection applicants cancelled claims 2-4, 46-60, 113, 114, amended claims 1, 9, 11, 84-88, 97, 98, 102, 103, 115, 127 and added new claim 129 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that applicants have amended the claims to recite point mutations H638 or F155 and that the claims are not drawn to all possible hyperactive reverse transcriptases comprising one or more point mutations.

Applicant's amendment of the claims and applicants complete traversal is acknowledged and has been carefully considered, however, is found non-persuasive on the following basis.

While applicants have now amended the claims to recite that the claims are limited to a hyperactive M-MLV reverse transcriptase comprising a point mutation in the processivity domain corresponding to H638 and a point mutation in the nucleotide selection domain corresponding to F155, it remains that applicants have not limited the claimed transcriptase mutants structurally, such that the claimed genus is extremely broad as it is truly only limited by function. While applicants do reference point mutations corresponding to H638 and F155, it remains that this is the only structural limitation in the claim and even this "structural limitation" is somewhat unclear . As such it remains that applicants have not adequately described the claimed genus of mutant reverse transcriptases.

The specification fails to describe additional representative species of these reverse transcriptases by any identifying structural characteristics or properties other than the activities recited in claims 1, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear,

concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. It is noted that newly added claim 129 does not correct any of the above, as it is directed to a mutant reverse transcriptase comprising an amino acid sequence of SEQ ID NO: 2, and SEQ ID NO: 2 comprises many small amino acid sequences.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 5-9, 11-28, 84-98, 102-112,115-125 and 127-129 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the M-MLV reverse transcriptase comprising the amino acid sequence of SEQ ID NO: 2 consisting a mutation at position H638 and F155, does not reasonably provide enablement for any hyperactive M-MLV reverse transcriptase protein comprising a point mutation in the processivity domain corresponding to H638 and a point mutation in the nucleotide selection domain corresponding to F155. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1-9, 11-28, 46-60, 84-98, 102-125 and 125-128. In response to this rejection applicants cancelled claims 2-4, 46-60, 113, 114, amended claims 1, 9, 11, 84-88, 97,

98, 102, 103, 115, 127 and added new claim 129 and traverse the rejection as it applies to the newly amended claims.

As above, applicants traverse the rejection on the basis that applicants have amended the claims to recite point mutations H638 or F155 and that the claims are not drawn to all possible hyperactive reverse transcriptases comprising one or more point mutations.

As above, applicant's amendment of the claims and applicants complete traversal is acknowledged and has been carefully considered, however, is found non-persuasive on the following basis.

As above, applicants have now amended the claims to recite that the claims are limited to a hyperactive M-MLV reverse transcriptase comprising a point mutation in the processivity domain corresponding to H638 and a point mutation in the nucleotide selection domain corresponding to F155, it remains that applicants have not limited the claimed transcriptase mutants structurally, such that the claimed genus is extremely broad, as it is truly only limited by function. While applicants do reference point mutations corresponding to H638 and F155, it remains that this is the only structural limitation in the claim and even this "structural limitation" is somewhat unclear . As such it remains that applicants have not sufficiently enabled the claimed genus of mutant reverse transcriptases.

The specification continues to not support the broad scope of the claims which encompass all modifications and fragments of any the mutant M-MLV reverse

transcriptase comprising a point mutation in the processivity domain and a point mutation in the nucleotide selection domain, corresponding to H638 and F155, respectively, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the hyperactivity; (B) the general tolerance of M-MLV reverse transcriptases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a reverse transcriptase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the reverse transcriptase activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having the claimed reverse transcriptase activity.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any modification and fragment of any mutant M-MLV reverse transcriptase comprising a point mutation in the processivity domain and a point mutation in the nucleotide selection domain, corresponding to H638 and F155, respectively. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient

guidance, determination of those mutant reverse transcriptases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 129 is rejected under 35 U.S.C. 102(b) as being anticipated by Gao et al. (U.S. Patent No. 6,136,582).

Gao et al. teach a hyperactive Moloney murine leukemia Virus reverse transcriptase comprising a mutation at position 155 of the wild-type polymerase. The taught polymerase has a DNA polymerase activity of between 0.1 and 300 Units per microgram and RNase H activity between 0.1 and 25 percent of the wild-type RNase H activity. Gao et al. further teach kits for nucleic acid synthesis comprising the above hyperactive reverse transcriptase and reaction buffers, primers, nucleotides, instructions etc...

As such Gao et a. teach an isolated reverse transcriptase protein comprising an amino acid sequence of SEQ ID NO: 2. It is recognized that the amino acid sequence

of SEQ ID NO: 2 comprises many smaller amino acid sequences within the full-length of SEQ ID NO: 2, many of which are found in the Moloney murine leukemia Virus reverse transcriptase of Gao et al., such as YVDD (See position 223-226 of instant SEQ ID NO: 2).

***Conclusion***

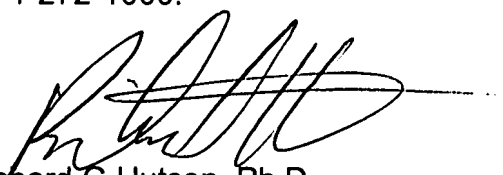
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
11/29/2007